Meridian Medical Technologies®, Inc.
1945 Craig Road
St. Louis, MO 63146

October 31, 2017

Miguel A. Hernández
Director, Compliance Branch
US Food and Drug Administration
8050 Marshall Drive, Suite 205
Lenexa, KS 66214

RE: Meridian Medical Technologies, Inc. / FEI Number: 1950222
Quarterly Action Plan Update for 3rd Quarter 2017 – Inspection Response Status

Dear Mr. Hernández:

In the April 14, 2017 response to the Food and Drug Administration ("FDA") Form 483 issued March 24, 2017, Meridian Medical Technologies, Inc. ("MMT") included a commitment to provide FDA with Quarterly Updates with respect to the 483 response commitments. Also in the response, MMT committed to working with a third party consultant to develop a Compliance Action Plan ("CAP") which would ensure a holistic response to the 483 observations as well as the broader GMP subsystems implicated by the Observations. Additionally, after receiving the FDA Warning Letter on September 05, 2017, MMT made additional commitments in the September 26, 2017 Warning Letter Response regarding specific deliverables we would communicate to FDA via these quarterly updates. These Warning Letter Response commitments were also added to the CAP.

In regards to the Warning Letter response deliverables committed to in this specific quarterly update, MMT stated it would; 1) Provide the CAPA outcomes and planned completion dates from the Phase II CAP third party assessments that were conducted during the 3rd quarter of 2017, 2) Provide a plan for a retrospective review that would be conducted under protocol for 'other failures or discrepancies that did not result in manufacturing investigations, such as multi-tiered specifications for incoming or finished goods', and 3) Provide a detailed timeline for EpiPen design verification which would be developed based on product life cycle design assessments.

The Phase II CAP deliverable of completing 3rd party audits of Management Responsibility, Corrective and Preventative Actions, and Purchasing Controls were completed in accordance with the plan timeline. Furthermore, MMT determined applicable CAPA and assigned associated target completion dates for each CAPA. These additional CAPA have been added to the CAP under Appendix 1 version 3.0 (Exhibit 1) and are also included in the most current CAP dashboard (Exhibit 2). It should be noted that all eighty-seven (87) CAPA items completed in the CAP have been finished on or before their target due date. MMT currently has eleven (11) CAPA coming due in the next 21 calendar days and one (1) CAPA that has been identified to management as being at risk of missing the target due date.

In response to observation 13B of the 483, MMT committed to complete the revalidation of the EpiPen process end to end, including improvements made to the (b) (4) (i.e. (b) (4) (b) (4) and extension of (b) (4) The revalidation was targeted to be completed by December 15, 2017 based on the plan to implement the changes during (b) (4) planned for (b) (4) To (b) (4) (b) (4) was (b) (4) (b) (4) (b) (4) Currently, MMT is scheduled to complete the process validation activities on December 15, 2017, but there is a possibility that the revalidation will not be complete in December if there are unforeseen schedule delays or processing deviations. We will update FDA on the status of this action in the next quarterly update.

MMT has developed a plan to perform a retrospective review for;

- 'other failures or discrepancies that did not result in manufacturing investigations, such as multi-tiered specifications for incoming or finished goods',
- MMT is providing the following schedule; MMT will identify all products still within expiry and evaluate if there was any acceptance testing results outside the tier 1 (b) (4) limits for the finished goods or the components within them.

For any lots identified with incoming components that have been released with individual results outside of tier 1 limits, MMT will develop a Health Hazard Assessment to determine potential patient risk. This activity will be performed under protocol, with the protocol assessing data for all Epinephrine products and associated incoming components created by **December 15, 2017**. An assessment of potential impact to patient safety will be performed and a final report will be completed which summarizes these findings. The final report will be completed **by February 28, 2018.** All other products manufactured by MMT and still within shelf life will be evaluated under separate protocols following the same plan and criteria for execution. The protocols for remaining products will be created by **January 15, 2018**. All associated final reports will be completed **by April 30, 2018.**

A detailed timeline for EpiPen design verification has been developed. This timeline was based on product life cycle design assessments and is included as Exhibit 3.

Please note that this letter and the corresponding attachments contain confidential information related to MMT's business operations and processes and accordingly are not subject to disclosure under the Freedom of Information Act, 5 USC 552(b)(4) and 21 C.F.R 20.61(a)-(b).

Sincerely,

Jeffrey A. Schramer
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(1)
James A. Donovan
Site Leader
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cc: Cheryl Bigham
District Director, Kansas City District Office

(1) See attached signature page sent to Site Leader/Designee for review and approval via scanned copy on 31 Oct 2017.
J A Schramer 31 Oct 2017

A detailed timeline for EpiPen design verification has been developed. This timeline was based on product life cycle design assessments and is included as Exhibit 3.

Please note that this letter and the corresponding attachments contain confidential information related to MMT's business operations and processes and accordingly are not subject to disclosure under the Freedom of Information Act, 5 USC 552(b)(4) and 21 C.F.R 20.61(a)-(b).

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(1)

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James A. Donovan by JOHN F ADDY as DELEGATE

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cc: Cheryl Bigham
District Director, Kansas City District Office

(1) See prior page for SQOL Approval. Site Leader delegate J. Addy reviewed a scan of original.
31Oct2017

Exhibit 1. Compliance Action Plan (CAP) – (approved 30Jun2017) with Most Current CAP Appendix I (last updated October 30, 2017)

Compliance Action Plan (CAP)

for:

Meridian Medical Technologies, Inc.
St. Louis, MO

June 29, 2017

Prepared By / Date:

J A. Schramer 29 Jun 2017

Jeffrey A. Schramer
Site Quality Leader, MMT

Approved By / Date:

29 JUNE 2017

Tom Handel
President and General Manager, MMT

Approved By / Date:

(1)

Kevin Jenkins
Vice President of Quality Excellence, Pfizer Corporation

(1) See signed cover page of emailed scan. Scan signed by K. Jenkins on 30 Jun 2017. J A. Schramer 26 Jul 2017

Compliance Action Plan (CAP)

for:

Meridian Medical Technologies, Inc.
St. Louis, MO

June 29, 2017

Prepared By / Date:

Jeffrey A. Schramer
Site Quality Leader, MMT

Approved By / Date:

29 JUNE 2017

Tom Handel
President and General Manager, MMT

Approved By / Date:

30 June 2017

Kevin Jenkins
Vice President of Quality Excellence, Pfizer Corporation

Index

1. INTRODUCTION

Meridian Medical Technologies, Inc., a Pfizer Company (hereafter MMT) located at St Louis, MO, was inspected by the U.S. Food and Drug Administration (FDA) from February 20 through March 24, 2017. At the conclusion of the Agency's inspection on March 24, 2017, MMT received a Form 483 with 14 multi-part observations relating to the manufacture of the firm's auto-injector combination products.

MMT submitted a written response to the Form 483 on April 14, 2017. Within the response was a commitment to engage a third party consultant that specializes in Quality System Remediation. To that end, (b) (4) was retained by MMT as the identified 3rd party in May 2017. Specifically, (b) (4) involvement was to review and provide input to this document, to conduct in-depth audits of the three (3) priority topics listed directly below in the next paragraph, and to identify the topics/areas listed under Section 5 that are in need of a rigorous audit, in order to establish the level of compliance.

One of the deliverables within the 483 Response, was for MMT to create a Compliance Action Plan (CAP). It was communicated within our 483 response that the CAP would focus on three key areas for assessment by the 3rd party, which would then result in corresponding improvement commitments by MMT. The following systems communicated to be further assessed by a 3rd party are:

- Design Controls
- Complaint Investigations
- AQLs (Sampling Plans)

Furthermore, the 483 Response stated the CAP would include any new commitments that arise from gap assessments/reviews performed as part of the 483 response commitments, as well as any additional quality systems requested for evaluation by a 3rd party consultant.

2. PURPOSE

The CAP is intended to document corrective and preventive actions arising from assessment work described above, in addition to the commitments previously provided in MMT's original April 14, 2017 483 Response. This CAP supplements the Form 483 response and provides assurance that a comprehensive, holistic approach is being taken by MMT. The CAP will also be utilized to document corrective and preventative action effectiveness checks (which will be conducted by a 3rd party) for all commitments within the CAP.

The in depth 3rd party assessments of existing systems and CAPA effectiveness verification work will follow completion of the initial version of this CAP. CAP Appendix I will be updated on at least a quarterly basis to provide tracking information to the

compliance initiatives stated within the CAP and each update will be approved by management.

3. GOVERNANCE AND OVERSIGHT

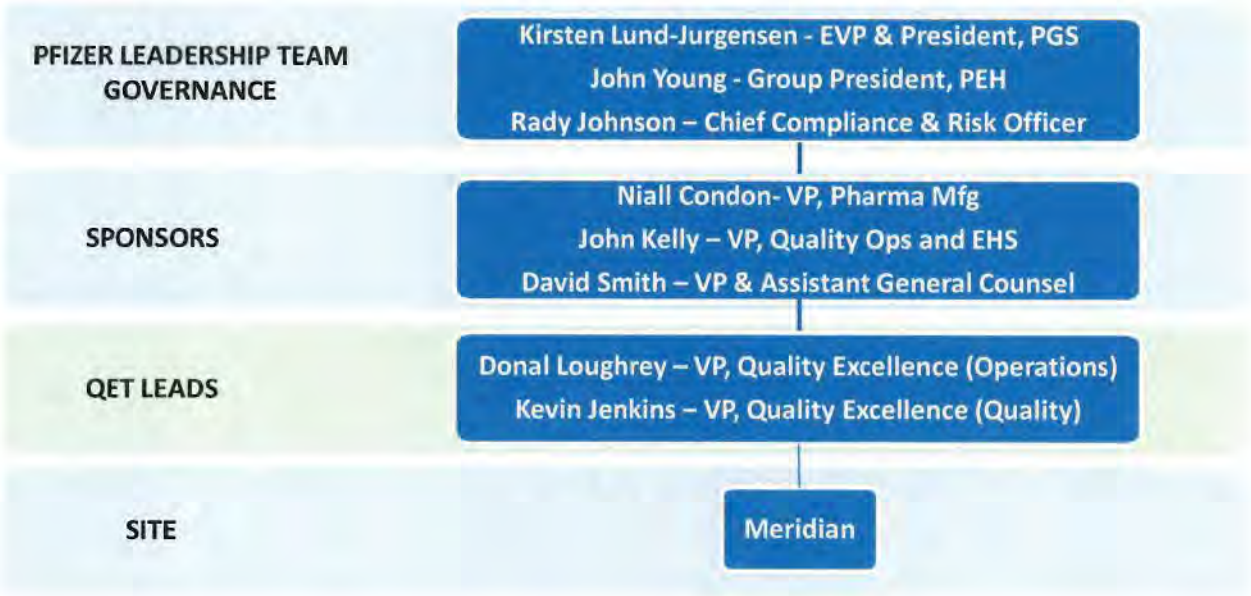
In order to provide focused resources for manufacturing sites undergoing remediation, Pfizer established a Quality Excellence Team (QET) to provide focus and support on improvement at sites undergoing remediation in May 2017. The QET is co-led by Operations and Quality, with dual reporting to the VP Pharmaceutical Manufacturing Operations and the VP Quality Operations and Environmental Health & Safety and accountability to Pfizer's Leadership Team Governance as described below.

The objective of the QET is to deliver a focused and aligned approach to development and execution of quality improvement activities at selected network sites in order to achieve/maintain Voluntary Action Indicated (VAI) status. The team's responsibilities include the following:

- Ensuring comprehensive quality improvement plans for each site in scope are in place and incorporate actions and recommendations from regulatory inspections and internal/external assessments
- Providing above site project management, as well as frequent updates to sponsors
- Ensuring projects are prioritized and resourced appropriately and programs/training are developed as needed
- Accelerating key projects and driving overall timelines, ensuring regulatory commitments are made
- And ensuring consistency for specific improvements applicable across multiple sites.

The integration of the CAP deliverables into the QET Oversight and Governance process are further described in the Communication section of this document.

Below is the governance structure of the QET:



4. APPROACH AND METHODOLOGY

Development of this CAP included (b) (4) review of the Form 483 observations, MMT's responses, physical inspection/tours of buildings and facilities, performing reviews of records and procedures, and conducting interviews with MMT management and key staff personnel.

5. CAP SCOPE AND TIMING

As described in the FDA response commitment letter, MMT previously identified three key areas for improvement that will be a primary focus of the 3rd party assessments required for the CAP, namely:

- Design Controls
- Complaint Investigations
- AQLs (Sampling Plans)

Additionally, other areas / topics for evaluation were identified by either MMT or (b) (4) through staff interviews, document reviews and facility tours that were conducted by (b) (4) during the weeks of May 15, May 22, and June 5, 2017. A tiered risk-ranking was performed for all the topics identified. Risk was predicated on potential impact to patient safety, product quality, pre-existing internal assessments/improvement plans, and/or regulatory compliance. Other factors

considered with respect to risk were: whether the issues identified by FDA and MMT's proposed corrective actions appeared to have a comprehensive approach toward resolution as described in the MMT 483 response (per (b) (4) evaluation of MMT's 483 response), whether the issues within the FDA 483 were one-off occurrences vs. systemic cause; or other factors that suggested a comprehensive evaluation was warranted. The priorities for the comprehensive evaluations to be conducted by the 3rd party are below, and separated into two phases. (b) (4) has been contracted to perform the PHASE I evaluations. Below are the quality systems and timelines expected for PHASE I and PHASE II:

PHASE I ((b) (4) Assessments of the PHASE I topics below are expected to be completed by July 15, 2017, and the corresponding MMT CAPAs to be identified by July 30, 2017)

- Design Controls
- Complaint Investigations
- Investigations System
- AQLs (Sampling Plans)

PHASE II (3rd Party Consultant Assessments to be completed by October 1, 2017, and the corresponding MMT CAPAs to be identified by October 31, 2017)

- Management Responsibility
- Corrective and Preventive Actions
- Purchasing Controls

6. PROJECT OVERVIEW

The objectives of this CAP will be achieved by completion of the following key steps:

- **In-depth 3rd Party Assessments:** Completion of a series of in-depth audits by third party consultant, focusing on the Phase I and II topics listed in Section 5.
- **483 Commitment Internal Assessments:** MMT or Pfizer Corporate will perform internal Pfizer assessments per the original 483 response commitment schedule. PHASE I and PHASE II topic audits will not be conducted by MMT/Pfizer.
- **Report:** Preparation of an audit report for each of the topics/systems assessed by third party consultant or assessed internally will be issued.
- **CAPA Determination:** MMT will review each Report and determine appropriate CAPA, as necessary.
- **CAPA Implementation:** MMT will track implementation of corrective or preventive actions (CAPA) through its electronic CAPA tracking system
- **Effectiveness Checks:** Evaluation of all CAPA through effectiveness checks will be performed by a 3rd party consultant.

7. THIRD PARTY AUDIT DETAILS

A more detailed description of the comprehensive 3rd party evaluations described within Section 5 Phase I and II is as follows:

1. Completion of a series of in-depth audits. 3rd party to conduct comprehensive cGMP audits to determine compliance with the relevant aspects of 21 CFR Parts 210 and 211, and Part 820 as described in Part 4.4. (Combination Products). For each individual audit, a detailed audit plan/agenda topics will be prepared.

2. Preparation of detailed audit reports. Each audit report shall include an executive summary of the key observations and will provide an aggregate overview of the audit findings ranked based upon risk (critical, major or minor). The audit report shall incorporate a set of recommendations that, if implemented successfully, will provide a high degree of assurance for sustained compliance with cGMP, and overall conclusions regarding the state of compliance. This audit report is to be completed by the consultant.

3. CAPA dialogue and documentation. MMT will engage the 3rd party in discussions on recommended CAPA where necessary. MMT will issue an internal audit response report to each 3rd party audit report. The response report will include MMT's final CAPA planned for implementation as a result of the audit (where applicable). Each internal audit response report will be approved by the MMT Site Quality Operations Leader. The outcome of each audit will be reported up through the Quality Excellence Team and its sponsors through the governance process.

8. CORRECTIVE AND PREVENTATIVE ACTIONS

1. Implementation of corrective or preventive actions. All CAPA documented within Appendix I of this CAP are derived from three different sources: 1) CAPA implemented as the result of the 3rd party audits carried out under this CAP (source listed as "CAP"); 2) CAPA as a result of internal assessments performed as a result of the April 2017 FDA 483 response commitment (source listed as "CAP"), or 3) CAPA listed directly in response to the April 2017 Form 483 response or provided to FDA at the March 24, 2017 close-out meeting (source listed as "FDA Audit"). The source of each CAPA will be documented within Appendix I of the CAP, along with the target completion date

2. Management Oversight. MMT will publish a (b) (4) report listing the current status of CAPA items within this CAP. The report will be issued to MMTs' Management with Executive Responsibility and the leaders of the Pfizer Corporate Quality Excellence Team.

3. Evaluation of CAPA through effectiveness checks. CAPA effectiveness checks must be performed after a sufficient implementation period. The results of these effectiveness checks are to be documented via audit reports prepared by a 3rd party consultant. This will consist of a rolling set of focused audits and/or evaluation of performance data to verify CAPA implemented did not result in repeat problems and/or unintended issues that are not compliant with cGMP. The target for these effectiveness checks should be approximately (b) (4) post CAPA closure. Status and results of the effectiveness checks will be documented within Appendix I of the CAP.

9. COMMUNICATION

A Steering Committee comprised of leadership with executive responsibility for MMT and QET Leads will meet (b) (4) to discuss progress on the Compliance Action Plan.

Standing agenda for the (b) (4) meetings are to include:

- Action Items
- CAPA Commitment Dashboard
- (b) (4) Snapshot (recently completed activity and look ahead to the coming actions)
- Staffing Update
- Discussion Items
- Any specific commitment detail that needs Governance visibility/alignment
- Routine Quality Performance - Investigation Status

The CAP APPENDIX I will be updated on a (b) (4) The CAP and the newly updated APPENDIX I will be provided to the FDA within one month following the (b) (4) update of APPENDIX I, until such time that all 483 Response and CAP related CAPA are completed along with successful effectiveness checks.

10. CRITERIA FOR SUCCESS:

Criteria for determining project success include, but are not limited to, the following:

- Identified corrective/preventive actions (audit recommendations) that will allow MMT to attain/sustain substantial compliance with cGMP.
- A reduced potential for product and/or regulatory compliance risk.
- A high degree of assurance for future, successful FDA and health care authority inspections.
- Reaching and maintaining a quality mindset at all levels within the organization.

APPENDIX I
Compliance Action Plan Related CAPA Status
(Version **3.0** Updated Date- **30 October 2017**)

APPENDIX I Update Prepared By / Date:

Nicole Typaldos 30OCT2017

Nicole Typaldos
Quality Systems Manager, MMT

APPENDIX I Approval By / Date:

Jeffrey A. Schramer 30OCT2017

Jeffrey A. Schramer
Site Quality Operations Leader, MMT

Table I **Third Party Assessment Tracking**

Topic	3rd Party Auditor	Audit Status	Audit Report Target Date	Audit Report Completion Date	MMT Response Target	MMT Response Completion Date
Design Controls	(b) (4)	Complete	15Jul2017	14Jul2017	30Jul2017	30Jul2017
Complaint Investigations		Complete	15Jul2017	14Jul2017	30Jul2017	30Jul2017
Investigations System		Complete	15Jul2017	14Jul2017	30Jul2017	30Jul2017
AQLs (Sampling Plans)		Complete	15Jul2017	14Jul2017	30Jul2017	30Jul2017
Management Responsibility		Not Started	01Oct2017	30Sep2017	31Oct2017	30Oct2017
Corrective and Preventative Action		Not Started	01Oct2017	30Sep2017	31Oct2017	30Oct2017
Purchasing Controls		Not Started	01Oct2017	30Sep2017	31Oct2017	30Oct2017

Table II FDA 483 Related Corrective and Preventative Action Tracking, by order of Observation and Due Date

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	Cover Letter	MMT will engage SME's within the Pfizer / Meridian / Industry network and experienced independent consultants with significant experience with medical device quality systems to develop a Compliance Action Plan (CAP) that will identify corrective and preventative actions that will enhance our systems and processes. The CAP will focus on three primary areas for improvement, as identified in the observations and out own internal discussions: Design controls (including DHF) Complaint Investigations Acceptable Quality Limits (AQL)	15-Jun-17	15-Jun-17	Quality Systems		
FDA Inspection	Cover Letter	Submit updates to FDA on a quarterly basis, with the first update to be submitted by July 30, 2017 (for the three month period ending June 30, 2017). First Update will include a copy of our CAP.	30-Jul-17	30-Jul-17	Quality Systems		
FDA Inspection	1, 4, 6, 8	Update the standard sampling plan for EpiPen finished good functionality test to (b) (4) units per assembled lot, reduce AQL from (b) (4) to (b) (4) The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) for assembled final product functionality testing. The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) for product release testing. (See Response 6A table 4) The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) for product release testing. (See Response 6A table 4) (b) (4) AQL applied for release testing will be instituted For those essential functional attributes as design inputs and outputs are confirmed critical through risk assessment process, a (b) (4) (b) (4) AQL for determination of sample size will be applied for release testing reflecting system level reliability.	30-Apr-17	28-Apr-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	1, 13	SOP-QLA-MQA-00720 to be updated to assure consistent application across lots in the scope of an investigation when additional testing is performed to evaluate potential quality impact SOP-QLA-MQA-00720 will be revised to require that all on-going preventative actions that address root cause are included in an investigation report SOP-QLA-MQA-00720 will be revised to require that deviation investigators implement the use of trend tools such as control charts to identify when the item or event being investigated differs from historical process trend as an aid in the investigation process SOP-QLA-MQA-00720 will be revised to include an instruction that the potential impact of reprocessing or atypical environmental conditions, such as (b) (4) be considered during relevant investigations	31-May-17	30-May-17	Quality Systems		
FDA Inspection	1	Update SOP-QLA-MQA-00004 to ensure that formal notification to management occurs for any OOS result, whether it be for a finished product, in-process sample, or incoming component	31-May-17	30-May-17	Quality Systems		
FDA Inspection	2	SOP-MAN-INS-00029 will be updated to add specific requirements for the simulation of fatigue conditions during inspector qualification/re-qualifications for all product lines	31-May-17	19-May-17	P&I		
FDA Inspection	2, 14	New Job Aid to be created which includes visual examples and further details for the steps performed during the (b) (4) New OJT training document will be developed and implemented for all colleagues that perform (b) (4) The new OJT will require review of the job aid, review of SOP-PRO-CLP-00005, and hands on training (New Job Aid to be created which includes visual examples and further details for the steps performed during the pre-use evaluations of (b) (4)	7-Jun-17	2-Jun-17	Aseptic Operations		
FDA Inspection	2	MVI performance improvement: (b) (4) to further improve (b) (4) (b) (4) (b) (4) for inspectors. – ATNAA	30-Jun-17	23-Jun-17	P&I		
FDA Inspection	2	AQL sampling will be adjusted so that results of the sampling are (b) (4) (b) (4) This will enable direct and immediate performance feedback (b) (4) – ATNAA	31-Jul-17	28-Jul-17	P&I		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	2	MVI performance improvement: An attribute analysis capability study for the ATNAA/DuoDote MVI process will be performed. Any improvement opportunities will be incorporated into a process continuous improvement plan	31-Aug-17	31-Aug-17	P&I		
FDA Inspection	2	(b) (4) will be implemented for (b) (4) (b) (4) performance on a defined frequency	30-Nov-17		P&I		
FDA Inspection	3	Statistical Analysis with (b) (4) of complaint data for all products and all complaint sub-classes. Based on the analysis, statistically based lot trend alert limits will be identified for complaint sub-classes.	15-May-17	15-May-17	Complaints		
FDA Inspection	3, 13	SOP-QLC-QLE-00702 will be revised to clarify that site personnel can and should take action to address any combination of complaints, no matter the number, that appears to signal a trend or issue and to establish the following expectations with respect to alert limits: - statistically based alert limits for the number of complaints of a similar nature for the same lot for all products and all complaint sub-classes - a requirement that lot trend alert limits are based on statistical analysis of historical complaint data - a requirement that the statistically based lot trend alert limits be reviewed (b) (4) SOP-QLC-QLE-00702 will be revised to include an instruction that the potential impact of reprocessing or atypical environmental conditions, such as (b) (4) be considered during relevant investigations	31-May-17	31-May-17	Complaints		
FDA Inspection	3	Pfizer corporate procedure GPB-QS1073 will be updated to clarify the purpose of the expedited complaint process. As part of the update, all complaint classifications associated with devices and combination products will be evaluated to ensure alignment to the requirements of the specific regulatory notifications described above. In addition, all complaint classifications associated with the products manufactured at MMT will also be evaluated to ensure that any product specific exceptions regarding prioritization are included in the update to GPB-QS1073.	30-Jun-17	30-Jun-17	Complaints		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	3	SOP-QLC-QLE-00702 will be updated to reflect the clarifications in GPB-QS1073 regarding the purpose for expediting complaints	15-Jul-17	15-Jul-17	Complaints		
FDA Inspection	3	Risk Assessment will be performed including Safety/Medical/Clinical, to document the rationale for the ranges of the essential performance inputs and their criticality/severity based on the emergency, life-saving intended use of the product. The risk assessment will also establish acceptable mean complaint rates and will be reviewed at a minimum of annually as part of the Annual Product Review	31-Jul-17	28-Jul-17	Complaints		
FDA Inspection	3	Engaging experienced independent consultants with significant experience with medical device quality systems to conduct an assessment of the MMT quality systems, including Complaint Management. Assessment	31-Aug-17	25-Jul-17	Quality Systems		
FDA Inspection	3	Creation of Action Plan with timeframe for corrective actions (from consultant assessment of Complaints)	30-Sep-17	29-Sep-17	Complaints		
FDA Inspection	4	New procedure to conduct routine Machine Capability studies has been drafted and will be approved. (SOP-QLA-GEN-11104)	15-May-17	15-May-17	Operational Excellence		
FDA Inspection	4	A detailed roll-out plan for all equipment to be studied will be approved by Manufacturing and Quality. The initial Machine capability study to be conducted under the scope of the new procedure will be for the filling equipment for ATNAA. Machine Capability studies will be performed on the (b) (4) Filler equipment.	30-May-17	30-May-17	Operational Excellence		
FDA Inspection	4	Procedure will be developed by Operational Excellence, Manufacturing, and Quality to require routine in-process trending for ATNAA and EpiPen and to assess performance variability A new procedure will be developed by MMT to require routine in-process data trending of critical parameters to assess performance variability for ATNAA and EpiPen	30-Jun-17	23-Jun-17	Operational Excellence		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	4	Risk assessment, including representatives from the Safety/Medical/Clinical groups to document essential attributes for intended use and their criticality.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	4	In-process trending at the site will be in place for identified critical processing areas. A review of these trend reports will be incorporated into periodic reviews in the APRR.	30-Aug-17	29-Aug-17	Quality Systems		
FDA Inspection	4	In-process trending at the site will be in place for identified critical processing areas. A review of these trend reports will be incorporated into periodic reviews at SQRT.	30-Aug-17	28-Aug-17	Quality Systems		
FDA Inspection	4	Updates to the Process Maps are also being developed for current the products currently being manufactured at the site, ATNAA, to identify process input variables that can be further evaluated to enhance process capability. (ATNAA Filling)	31-Aug-17	31-Aug-17	Operational Excellence		
FDA Inspection	4	Trend (b) (4) for multiple lots and will develop action limits based upon process capability.	31-Aug-17	31-Aug-17	Operational Excellence		
FDA Inspection	4	Updates to the Process Maps are also being developed for current the products currently being manufactured at the site, ATNAA, to identify process input variables that can be further evaluated to enhance process capability. (ATNAA P&I)	31-Aug-17	31-Aug-17	Operational Excellence		
FDA Inspection	4	For those essential characteristics that are confirmed in the risk assessment and defined as critical in Table 2 of Response 6A, there will be a plan implemented to conduct testing based on system level reliability.	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	4	Add action limits from trended eject levels to EpiPen Assembly process batch records	30-Sep-17	29-Sep-17	P&I		
FDA Inspection	4	Add action limits from trended eject levels to ATNAA Assembly process batch records	30-Sep-17	29-Sep-17	P&I		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	4	Trend reporting, including ejects from the (b) (4) machine, will be incorporated into periodic reviews at Site Quality Review Team (SQRT) meetings for continuous improvement	31-Oct-17	05-Sep-17	Quality Systems		
FDA Inspection	4	Trend reporting, including ejects from the (b) (4) machine, will be incorporated in the Annual Product Records Review (APRR) for continuous improvement	31-Oct-17	19-Oct-17	Quality Systems		
FDA Inspection	4	As an outcome of the capability studies, Six-Sigma projects will be employed to reduce variability where improvement areas are identified. Results from the capability studies will be incorporated into periodic reviews of Site Quality Review Team.	28-Feb-18		Quality Systems		
FDA Inspection	4	As an outcome of the capability studies, Six-Sigma projects will be employed to reduce variability where improvement areas are identified. Results from the capability studies will be incorporated in the Annual Product Record Review (APRR).	28-Feb-18	19-Oct-17	Quality Systems		
FDA Inspection	5	Complaint trend reports will be based on finished product lots, manufacturing dates, and component lots. These additional site trend reports will be presented in SQRT and incorporated in the APRRs to identify any corrective actions needed. A plan for implementing these additional reports (data collection method, procedures, etc.) will be developed and implemented thereafter.	15-Jul-17	14-Jul-17	Complaints		
FDA Inspection	6	Evaluate SOP-DVL-PRT-00002 procedure for potential updates to include the development of a system level reliability and to ensure linkage to the design outputs. The procedure will require the Design Input document, PRD/TRD, to include cross reference to the risk assessment and documentation supporting the individual design inputs. Training methodology using human performance tools will be developed to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6, 7, 8	Risk Management file will be updated with a risk assessment performed by a CFT including representatives from Safety/Medical/Clinical groups, to document essential attributes and their criticality and rationale for design inputs. Risk Management file will be updated with a risk assessment including representatives from Safety/Medical/Clinical to document the rationale for the ranges of the essential performance inputs and their criticality/severity based on the emergency, life-saving intended use of the product. The risk management file will be updated with a risk assessment including review by representatives from Safety/Medical/Clinical to document the rationale for the ranges of the essential performance inputs and their criticality based on the emergency, life-saving intended use of the product. Risk Management file will be updated with a risk assessment (states CFT (S/M/C) will be completed JUL2017) The risk management file will be updated with a risk assessment.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	MMT will evaluate potential (b) (4) of auto-injectors to include in reliability testing. System level reliability risk assessment will be completed	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	MMT will evaluate its design input procedures for potential updates to include development of system level reliability.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	The design inputs document will be updated for consistency between the product requirements section and the technical requirements section.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	Risk Management file will be updated with a risk assessment performed by a cross-functional team, including Safety/Medical, to confirm essential attributes and their criticality based on severity of harm and intended use of the combination product. The PRD/TRD design inputs document will be reviewed to ensure completeness and that the inputs are written in a non-conflicting or ambiguous way.	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6	PRD/TRD 16-001 rev 1, design inputs document, will be updated to include the system level reliability specification of (b) (4)%	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	6, 7	The PRD/TRD design input document will be updated to include cross reference to the risk assessment and documentation supporting the risk assessment conclusions. PRD/TRD design inputs document will be reviewed to ensure completeness and that the inputs are not written in a conflicting or ambiguous manner. MMT will update the PRD/TRD to trace the requirements to appropriate justifications and risk assessment. The design inputs document format will be revised to eliminate ambiguity between "Must" and "Want" design inputs. The "Wants" requirements of a PRD/TRD document will be removed from the document prior to finalizing design outputs such that design outputs can be traced directly to design in/out requirements. PRD/TRD 16-001 Rev1, injection through clothing is a requirement included as part of the use specification. This will be added to the Technical Requirement of the PRD/TRD design input document MMT will review the PRD/TRD, design inputs document, to ensure completeness and that the inputs and outputs are not written in a conflicting or ambiguous manner.	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	6	CFT (S/M/C) risk assessment completion. Risk control within the supply chain control plan will be evaluated to verify it supports the recommended system level reliability	31-Dec-17		Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6, 7	For those essential characteristics that are confirmed as critical in Table 2 of Response 6A, or modified per the safety/medical risk assessment, tiered specifications will be eliminated and replaced with a single range specification based on acceptable use for all EpiPen products including the [redacted (b) (4)] For those essential attributes that are confirmed critical through the risk assessment process, a single range specification, based on acceptable use For those essential functional attributes as described in Table 2, part 6A a single range specification based on User/Patient needs will be reassessed to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability. For those essential functional attributes as described in Table 2, part 6A a single range specification based on User/Patient needs will be reassessed to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability. These values will be applied to all relevant documents and the necessary updates will be made.	31-Dec-17		Design Controls		
FDA Inspection	7, 8	MMT will take the preventative action to evaluate SOP-DVL-PRT-00003 for linking design outputs to the design input requirements and the procedure will be updated as required to include a cross reference of design output conformance to design inputs. Training methodology using human performance tools will be used to assure adherence with the updated procedure. Evaluate SOP-DVL-PRT-00003 for linking design outputs to the design input requirements and the procedure will be updated to include evaluations of design output conformance to design inputs. Training methodology using human performance tools will be used to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	7	Design outputs will be reviewed to ensure completeness	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	7, 8	As part of our corrective action the design inputs requirements of PRD/TRD 16-001 Rev 1 will be updated to include the system level reliability requirement of (b) (4)% for essential performance requirements and (b) (4) This will be documented as a design output, in the engineering drawings: (b) (4) (b) (4) As part of our corrective action the design inputs requirements of PRD/TRD 16-001 Rev 1 will be updated to include the system level reliability requirement of (b) (4)% for essential performance requirements and (b) (4) This will be documented as a design output, in the engineering drawings: (b) (4) (b) (4) Reliability will then be defined in the design output and used to determine design verification requirements.	31-Aug-17	31-Aug-17	Design Controls		
FDA Inspection	8	Evaluate the design verification and validation procedure SOP-DVL-PRT-00004 for linking design verification requirements to the design input and output requirements. The procedure will be updated and training methodology using human performance tools will be used to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Evaluate the design control procedures for needed updates to ensure linkage of design verification requirements to the design input and outputs. Training methodology using human performance tools will be used to assure adherence with the procedure.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Design Control Procedures will be updated to require evaluation of (b) (4)	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Design inputs and outputs will be reviewed to ensure completeness.	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	8	MMT will develop through the risk assessment process the (b) (4) (b) (4) requirements for design verification and commercial process validation functional testing to be included as a component of the design verification and design validation plans. PRD/TRD 16-001 Rev 1 will be updated to include requirements for (b) (4) esting.	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	8	Execute a study with full functional system level reliability testing (for (b) (4) including (b) (4) of auto-injectors, if required, using auto-injectors produced as part of submission batches and (b) (4) in the warehouse for (b) (4) require functional system level reliability testing of the auto-injector device at end of product expiry, (b) (4) for future submission lots. For submissions made at less than full product expiry dating with on-going stability testing, a system level reliability test following (b) (4) (b) (4) may be included.	30-Sep-17	29-Sep-17	Design Controls		
FDA Inspection	9	Basic unit dFMEA will be approved.	31-May-17	25-May-17	Design Controls		
FDA Inspection	9	Basic unit dFMEA will be merged with the Auto-Injector dFMEA into a single document to consider the entire combination product device	31-Aug-17	31-Aug-17	Design Controls		
FDA Inspection	9	dFMEA risk assessment will be incorporated into the plant quality systems including (b) (4) Complaints, Change Control and for risk management.	15-Nov-17		Quality Systems		
FDA Inspection	9	The dFMEA reference 867935n will be reviewed at a minimum of annually as part of the APRR	28-Feb-18	19-Oct-17	Quality Systems		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	10	A new procedure to address preventive maintenance for the (b) (4) (b) (4) and the (b) (4) the auto-injectors (SOP-QLC-SQC-11108)	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394 will be revised by April 30, 2017 to require that the (b) (4) Employees will be re-trained on the revised procedure, which will also include re-training on the requirement to (b) (4) SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394, will be enhanced to provide specific instructions for the (b) (4) (b) (4) the performance of the test	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	Preventative maintenance procedures for all other equipment in the lab will be confirmed	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	A statistical study will be completed to evaluate (b) (4) (b) (4) for the functionality release testing for ATNAA and EpiPen. Action items will be established if any statistical differences are identified.	15-May-17	15-May-17	Operational Excellence		
FDA Inspection	10	A FMEA will be completed to identify and prioritize potential failure modes in the functional lot release test procedures and testing process. A plan to implement mitigating actions for any failure modes with unacceptable risk priority numbers.	15-Jun-17	15-Jun-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	10	A process has been developed for the (b) (4) Administrators to prompt and follow up with managers to create/modify curricula for new employees, new contingent staff or staff with job assignment changes. This process is already in place, but will be formally defined in a new (b) (4) SOP.	30-Jun-17	30-Jun-17	Quality Systems		
FDA Inspection	10	New (b) (4) will be (b) (4)	15-Jul-17	15-Jul-17	Laboratory		
FDA Inspection	10	SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394, will be enhanced to provide specific instructions for the proper technique to (b) (4) (b) (4) and the (b) (4) process. Visual aids will be added the SOPs to ensure consistency of practices for the (b) (4) test execution and data recording. The additional detail will describe what types of readings the operator can expect to see on the (b) (4) (b) (4)	31-Jul-17	28-Jul-17	Laboratory		
FDA Inspection	10	MMT curricula and curricula assignments for all colleagues will be reviewed by the responsible area manager or their designee to ensure assignments are correct and complete. This will be facilitated by Training Systems and area training staff and formally documented according to SOP-TRN-GEN-00044, curricula reviews will be completed (b) (4) thereafter.	31-Aug-17	31-Aug-17	Quality Systems		
FDA Inspection	10	MMT will evaluate the potential to modify the current (b) (4) to include a (b) (4) during the test. This would (b) (4) (b) (4)	30-Sep-17	29-Sep-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	11	SOP-LAB-MIC-00416 will be revised to also include this same holistic review of all lots that could be in scope of a sterility test failure, in accordance with SOP-QLA-MQA-00720	30-Jun-17	08-Jun-17	Laboratory		
FDA Inspection	12	(b) (4) will be performed to reaffirm all (b) (4) filling technicians' understanding of the required aseptic technique for removing (b) (4) This activity will be covered by (b) (4) and will take place prior to epinephrine filling production resumption	30-Apr-17	26-Apr-17	Aseptic Operations		
FDA Inspection	12	(b) (4) and/or specialized tools will be designed and implemented by the (b) (4) installation. These tools will better facilitate the (b) (4) from the (b) (4) Filler.	15-Jun-17	08-Jun-17	Aseptic Operations		
FDA Inspection	12	A (b) (4) on the (b) (4) Filler to protect the (b) (4) (b) (4) The (b) (4) in this area of the filling process will enhance (b) (4) (b) (4) and reduce potential for (b) (4) during the (b) (4) Smoke study and media fill will be performed as part of the (b) (4) omprehensive validation.	15-Jun-17	14-Jun-17	Aseptic Operations		
FDA Inspection	12	Procedures, documentation, and training associated with the action of (b) (4) from the (b) (4) will be enhanced at the (b) (4) mplementation. Applicable site personnel will train on this documentation update and the action will be added to the aseptic training program	15-Jun-17	13-Jun-17	Aseptic Operations		
FDA Inspection	12	Methods for loading all components on the (b) (4) Filler line will be evaluated by the corporate Microbial and Aseptic Support group by mid-June 2017	15-Jun-17	15-Jun-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	12	An action plan for other (b) (4) Filler line enhancements will be developed by July 1, 2017 as needed based on the findings of the evaluation	01-Jul-17	30-Jun17	Aseptic Operations		
FDA Inspection	12	A (b) (4) Filler to protect the (b) (4) (b) (4). The (b) (4) n this area of the filling process will enhance (b) (4) (b) (4) and reduce potential for (b) (4) during the (b) (4) Smoke study and media fill will be performed as part of the (b) (4) comprehensive validation.	20-Jul-17	19-Jul-17	Validation		
FDA Inspection	12	New production procedure will be created to include examples in which production lots would be aborted, such as machine inoperability requiring extensive maintenance work, break in asepsis, and non-sterile components running on the line	20-Sep-17	28-Aug-17	Aseptic Operations		
FDA Inspection	12	SOP-QLA-VAL-00020 will be revised to require each (b) (4) media fill to produce a minimum of (b) (4) for a required minimum total of (b) (4) units per media fill (b) (4) (dependent on (b) (4)	31-Oct-17	05-Sep-17	Validation		
FDA Inspection	12	MMT will engage SME's within Industry network with expertise in the design of (b) (4) to evaluate whether modifications can be made to the (b) (4) Filler, e.g. (b) (4) to reduce the risk of contamination during (b) (4) and all (b) (4) performed on the (b) (4) Filler.	31-Dec-17		Aseptic Operations		
FDA Inspection	12	Based on the conclusions of the evaluation (modifications to (b) (4) Filler), an action plan will be developed by January 31, 2018 to implement equipment modifications or other recommendations made by the expert.	31-Jan-18		Aseptic Operations		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	13	Current instructions on (b) (4) will be clarified to include when and how units should be protected, e.g. ensuring (b) (4) (b) (4) OP-MAN-INS-10154, RM-MAN-INS-10153, RM-MAN-INS-10152 and RM-MAN-PKG-10159 will be updated to include these instructions	15-May-17	15-May-17	P&I		
FDA Inspection	13	A (b) (4) study will be performed. The study will include measurement of (b) (4) at both the Brentwood and Westport facilities, including at the (b) (4) systems. During the study a group of test units and control units (b) (4) (b) (4) will be (b) (4) across the entire manufacturing process. (b) (4) will represent worse case conditions. Results from the test and control units will be compared to determine if any additional process (b) (4) controls should be implemented	30-Jun-17	29-Jun-17	Validation		
FDA Inspection	13	SOP-QLA-GEN-00802 will be revised to define requirements and provide examples for when to perform change effectiveness checks and risk assessments, specifically, for post-market design changes to combination products	31-Aug-17	30-May-17	Validation		
FDA Inspection	13	Full process validation from formulation through labeling of the assembled units will be completed (to establish a current baseline of the complete manufacturing process) – EpiPen	15-Dec-17		Validation		
FDA Inspection	13	Full process validation from formulation through labeling of the assembled units will be completed (to establish a current baseline of the complete manufacturing process) - ATNAA/DuoDote	29-Jun-18		Validation		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	n/a verbal	Update the MMT complaint SOP to signal a trend within a lot for the F2A complaint type based upon a review of historical complaint rates. Implement similar complaint rate signal limits for all expedited complaint types.	31-May-17	31-May-17	Complaints		
FDA Inspection	n/a verbal	Update Annual Product Records Review procedure SOP-QLA-MQA-00710 to include sections on: 1. Trending, tracking and in-process control charts for product defects 2. Process Capability Analysis	31-May-17	31-May-17	Quality Systems		
FDA Inspection	n/a verbal	Change acceptance criteria in the final product release batch records to require all individual units tested meet the (b) (4) lbs. average specification for (b) (4)	31-May-17	25-May-17	Laboratory		
FDA Inspection	n/a verbal	Automated vision systems for 100% inspection of the power pak (b) (4) (b) (4) will be put in place at (b) (4) machine. Vision system may be tied to (b) (4) system as a (b) (4) for sending the (b) (4) (b) (4) product.	20-Sep-17	20-Sep-17	Quality Systems		

Table III **CAP Related Corrective and Preventative Action Tracking as a Resulting from work completed under 483 commitments (by order of Due Date)**

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	Result of Obs. 10	A statistical study completed to evaluate (b) (4) variability for the functionality release testing for ATNAA and EpiPen. Laboratory to review recommended action and open corrective actions	15-Jun-17	15-Jun-17	Laboratory		
CAP	Result of Obs. 10	QC Device Lab Equipment PM Assessment: Create PM for (b) (4) (b) (4)	30-Jun-17	23-Jun-17	Laboratory		
CAP	Result of Obs. 10	QC Device Lab Equipment PM Assessment: Create PM for (b) (4) (b) (4)	30-Jun-17	23-Jun-17	Laboratory		
CAP	Result of Obs. 10	QC Device Lab Equipment PM Assessment: Create PM for (b) (4)	30-Jun-17	15-Jun-17	Laboratory		
CAP	Result of Obs. 10	Action item established for statistical differences identified. Operator	15-Aug-17	15-Aug-17	Laboratory		
CAP	Result of Obs. 10	Action item established for statistical differences identified. (b) (4)	15-Dec-17		Laboratory		
CAP	Result of Obs. 10	Mitigation Action - (b) (4) New (b) (4) will be evaluated to (b) (4) The (b) (4) will be determined (b) (4) (b) (4)	31-Dec-17		Laboratory		
CAP	Result of Obs. 4	Mitigation Action - (b) (4) The new upgrade of the data collection system will transfer the (b) (4) (b) (4)	31-Dec-17		Laboratory		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - Atropine (b) (4)	31-Jan-18		Operational Excellence		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - Pralidoxime Chloride (b) (4)	31-Jan-18		Operational Excellence		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - (b) (4) ATNAA	31-Jan-18		Operational Excellence		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	Result of Obs. 4	Machine Capability - Equipment Study - (b) (4)	31-Jan-18		Operational Excellence		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - (b) (4)	28-Feb-18		Operational Excellence		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - Final Assembly Machine - (b) (4) ATNAA	28-Feb-18		Operational Excellence		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - (b) (4) EpiPen	28-Feb-18		Operational Excellence		
CAP	Result of Obs. 4	Machine Capability - Equipment Study - (b) (4) EpiPen	28-Feb-18		Operational Excellence		
CAP	Result of Obs. 12	Enhance documents (BR, SOPs, etc.) and train colleagues on the discharging of components inside the grade A space. (i.e., (b) (4) (b) (4) etc.	31-Mar-18		Quality Systems		
CAP	Result of Obs. 12	Enhance procedures (SOP-PRO-FIL-00001) and train colleagues on proper aseptic behaviors for areas/processes identified as "critical" (i.e. during intervention, component loading, (b) (4) doors, etc.)	31-Mar-18		Quality Systems		
CAP	Result of Obs. 12	The interior of the new (b) (4) will be reclassified as Grade A space.	31-Mar-18		Laboratory		
CAP	Result of Obs. 12	Enhance the design of a sterile tool so (b) (4) (b) (4) (b) (4) (b) (4)	30-Jun-18		Aseptic Operations		
CAP	Result of Obs. 12	Enhance the design of a sterile tool used to keep the (b) (4) (b) (4) so that the operator does not reach over the open sterile cartridges when the (b) (4) (i.e. sterile tool, redesign of current (b) (4) etc.)	30-Jun-18		Aseptic Operations		
CAP	Result of Obs. 12	Enhance the design of a sterile (b) (4) to keep the operators hands away from the open empty glass cartridges. (i.e. sterile tool, redesign of current sterilizable tool with (b) (4) etc.)	30-Jun-18		Aseptic Operations		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	Result of Obs. 12	A dedicated surface will be designed and implemented for use within Room (b) (4) (b) (4) Filling (Epinephrine). (i.e., fold down table (or dedicated cart) which will be designated for use by (b) (4) operations). Applicable documents (SOPs, BR, etc.) will be updated added.	30-Jun-18		Aseptic Operations		
CAP	Result of Obs. 10	A FMEA completed to identify and prioritize potential failure modes in the functional lot release test procedures and testing process. A plan to implement mitigating actions for any failure modes with unacceptable risk priority numbers. Mitigating actions implementation expected 31JUL2017, and 31DEC2017 EFFECTIVENESS CHECK	31-Dec-18		Laboratory		
CAP	Result of Obs. 12	Redesign the (b) (4) loading method to enhance component dispensing within the (b) (4) Filler to reduce (b) (4) (b) (4) (i.e. (b) (4) (b) (4) etc.)	31-Dec-18		Aseptic Operations		
CAP	Result of Obs. 12	Redesign the (b) (4) Filler for enhanced component dispensing and (b) (4) mprovements.	31-Dec-18		Aseptic Operations		
CAP	Result of Obs. 12	Additional protection will be designed and implemented around the process for staged components without restricting (b) (4) (b) (4) (b) (4) etc.)	31-Dec-18		Aseptic Operations		

Table IV FDA Warning Letter Related Corrective and Preventative Action Tracking, by order of Observation and Due Date

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Drug CGMPs							
FDA Inspection	1	JA-DLV-PDV-10803 job aid will be updated to include specific detail on examining the safety release component related to this type of complaint by October 6, 2017.	06-Oct-17	06-Oct-17	Complaints		
FDA Inspection	1	Create a plan to conduct a similar (to that of SCAR) retrospective review, under protocol, of other failures or discrepancies that did not result in manufacturing investigations, such as multi-tiered specifications for in-coming or finished goods.	31-Oct-17		Quality Systems		
FDA Inspection	1	Conduct a comprehensive retrospective review of the manufacturing investigations for the site's other marketed products, pursuant to similar protocols. Significant findings from the retrospective reviews will be included in future quarterly updates to FDA.	01-Nov-17		Quality Systems		
FDA Inspection	1	CAPA will be initiated to evaluate potential changes to the device to eliminate this use-related error regarding the safe pin.	15-Nov-17		Design Controls		
FDA Inspection	1	Contract a third-party cGMP consultant to conduct batch record review for EpiPen batches, which will include a review of associated investigations, for [redacted] (b) (4) starting in November 2017.	30-Nov-17		Quality Systems		
FDA Inspection	1	SOP-QLC-QLE-00702, Product Complaint Handling, will be updated to include requirement for a formal risk assessment to assure that all potential patient hazards are considered as part of the root cause analysis and identified corrective actions.	30-Nov-17		Complaints		
FDA Inspection	1	SOP-QLA-MQA-00720, Event and Deviation Reporting (ER&QAR) will be updated to require that manufacturing investigations will be formally evaluated for their potential to impact patient use and safety as well as product quality. If the initial assessment concludes that there is potential impact to the device or device constituents, an SME will be required to review the investigation to ensure the investigation examines the deviation's impact to the batch as well as the impact to other batches.	30-Nov-17		Quality Systems		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	1	MMT will assess additional opportunities to enrich the current process for incorporating review of relevant adverse event data in conjunction with our pharmacovigilance team. This will be incorporated into existing MMT Site Quality Review Team ("SQRT") meetings and quality meetings that take place jointly with the pharmacovigilance team on a (b) (4) starting in November 2017.	30-Nov-17		Quality Systems		
FDA Inspection	1	Fill a new leadership role within the quality organization, Combination Product Program Director, to oversee quality and compliance including: Design Controls, Purchasing Controls and Quality Risk Management. This role has been posted and active recruitment is in progress.	31-Jan-18		Design Controls		
FDA Inspection	1	Execute protocol for failures or discrepancies that did not result in MIR for in-coming or finished goods.	31-Mar-18		Quality Systems		
FDA Inspection	1	Enhance the existing training program, with an emphasis on combination products and device requirements. The program will be developed with input from a third-party cGMP consultant.	31-Oct-18		Quality Systems		
FDA Inspection	1	MMT will establish an updated Quality Agreement with the Power Pak vendor to enhance its purchasing controls.	31-Oct-18		Quality Systems		
FDA Inspection	1	Assess need for continuing additional level of quality oversight of third party batch record review for EpiPen batches, which includes a review of associated investigations.	01-Nov-18		Quality Systems		
FDA Inspection	2	Form a cross-functional Complaints Analysis Trend Team. This team will analyze complaint trend data, support trend investigations including identification of CAPA and further refine complaint trend data presentation and statistical analysis.	01-Nov-17		Complaints		
FDA Inspection	2	GPB-QS1073, Prioritization of Pfizer Product Quality Complaint will be revised include EpiPen specific prioritization information in line with the Complaint Prioritization Protocol.	06-Nov-17		Complaints		
FDA Inspection	2	SOP-QLC-QLE-00702, Product Complaint Handling, will be revised to ensure that complaint investigation testing and techniques also consider potential patient risk and escalation where appropriate. Establish a link between the complaint trending process and review of the risk management file.	30-Nov-17		Complaints		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	2	SOP-QLC-QLE-00702, Product Complaint Handling will be revised to provide guidance to Complaint Investigators on verifying/assigning complaint subclasses to ensure consistent classification in support of accurate trending.	30-Nov-17		Complaints		
FDA Inspection	2	Conduct a retrospective assessment of all complaints received September 8. 2015, through September 7, 2017, that would now be classified as "expedited" instead of "high" or "normal" in order to confirm that the previous classifications did not have an impact on the completeness or outcome of the investigation.	30-Jan-18		Complaints		
Device QSR Requirements							
FDA Inspection	N/A	Conduct a comprehensive assessment of quality systems against the QSR with oversight and input from a third-party cGMP consultant.	31-Oct-18		Quality Systems		
FDA Inspection	1	Review supplier Quality Agreements for critical components identified in the dFMEA and work with these suppliers to develop appropriate control strategies for the identified high-risk components. These strategies may include the trending of critical quality attributes and a periodic review of supplier process capabilities by the SQRT.	01-Mar-18		Quality Systems		
FDA Inspection	2	Provide a plan for a detailed timeline for EpiPen design verification based on product lifecycle design assessments.	31-Oct-17		Design Controls		
FDA Inspection	2	Revise design verification procedure SOP-DVL-PRT-00004, Design Verification and Validation for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction, to reflect enhanced process and documentation in Design History File.	30-Nov-17		Design Controls		
FDA Inspection	2	To ensure alignment of design outputs to design inputs and design verification acceptability, MMT will execute a Design Traceability Matrix based on the requirements contained in SOP-DVL-PRT-00003, Design Outputs for New Products, Major Changes to Existing Products and Changes Affecting Product/ User Interaction	31-Oct-18		Design Controls		
FDA Inspection	2	Approve final report of design verification , including (b) (4) (b) (4) for the EpiPen NGA Auto-Injector.	31-Dec-18		Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	3	SOP-DVL-PRT-00004, Design Verification and Validation for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction will be updated to include all required design validation elements for combination products and to set forth the process for conducting design validation	30-Nov-17		Design Controls		
FDA Inspection	3	Develop a schedule for completing the activities for design verification for other approved products	30-Nov-17		Design Controls		
FDA Inspection	3	For EpiPen products: Comprehensive review of user needs	28-Feb-18		Design Controls		
FDA Inspection	3	For EpiPen products: Update risk analyses as appropriate	28-Feb-18		Design Controls		
FDA Inspection	3	For EpiPen products: Performing human factors formative studies as applicable	28-Feb-18		Design Controls		
FDA Inspection	3	For EpiPen products: Submit a human factors summative validation protocol, for review by the Agency	31-Mar-18		Design Controls		
FDA Inspection	3	Perform a pFMEA and integrate it into the site's overall risk management process.	31-Mar-18		Design Controls		
FDA Inspection	3	For EpiPen products: Execute the summative validation protocol	31-Oct-18		Design Controls		
FDA Inspection	3	For EpiPen products: Submit an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	31-Jan-19		Design Controls		
Quality Agreements							
FDA Inspection	N/A	As an improvement, MMT commits to conduct an assessment of its QA with Mylan by October 31, 2017. The goal of the assessment will be to identify opportunities to expand the current QA to improve express alignment with both QSR requirements and drug cGMP regulations.	31-Oct-17		Quality Systems		

Table V CAP Related Corrective and Preventative Action Tracking as a Result of 3rd Party Phase I Assessments (by order of Due Date)

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Compliance Action Plan – Design Controls Assessment & Statistical Methods Assessment						
CAP	R01-640, Truject Next Generation Auto-Injector (NGA) EpiPen Summary Report, will perform internal assessment of justification for the test results.	31-Oct-17		Design Controls		
CAP	SOP-DVL-PRT-00007, Design Transfer Requirements for New Products, Major Changes to Existing Product and Changes Affecting Product/User Interaction, will be updated for additional clarity and work instructions.	30-Nov-17		Design Controls		
CAP	Design Transfer Plan DTP-17-001 Rev 1, EpiPen Truject NGA [redacted] (b) (4) Design Transfer Plan, will be updated for additional clarity and inclusion of document references.	30-Nov-17		Design Controls		
CAP	SOP-DVL-PRT-00006, Design History File Requirements for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction, will be updated for additional clarity and work instructions.	30-Nov-17		Design Controls		
CAP	Equipment Specification Document for [redacted] (b) (4) (b) (4) will be revised to clarify/correlate the established definitions of the critical process control points.	30-Nov-17		Validation		
CAP	SOP-DVL-PRT-00002, Design Inputs for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction, will be updated to include additional clarity and work instructions.	30-Nov-17		Design Controls		
CAP	SOP-DVL-PRT-00003, Design Outputs for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction, will be updated to include additional clarity and work instructions.	30-Nov-17		Design Controls		

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	SOP-DVL-PRT-00005, Design Review for New Products, Major Changes to Existing Products, and Changes Affecting Product/User Interaction, will be updated to include additional clarity and work instructions.	30-Nov-17		Design Controls		
CAP	SOP-DVL-PRT-00004, Design Verification and Validation for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction, will be updated for additional clarity and work instructions.	30-Nov-17		Design Controls		
CAP	Design History File will be updated to include a "Usability File" and appropriate references/documentation.	30-Nov-17		Design Controls		
CAP	SOP-DVL-PRT-00001, Design and Development Planning Requirements for New Products, Major Changes to Existing Products and Changes Affecting Product/Use Interaction, will be updated to include a Design Traceability Matrix.	30-Nov-17		Design Controls		
CAP	SOP-QLA-MQA-00603, Proper Documentation, will be updated to include design verification and design validations within scope of the procedure.	18-Dec-17		Quality Systems		
CAP	SOP-QLA-VAL-10273, Project Validation Plan (PVP) and Report (PVR), and SOP-QLA-VAL-10270, Performance Qualification (PQ)/Process Validation (PV) Protocols and Reports – Equipment, will be updated for additional clarity.	18-Dec-17		Validation		
CAP	SOP-DVL-PRT-00001, Design and Development Planning Requirements for New Products, Major Changes to Existing Products and Changes Affecting Product/Use Interaction, will be updated to include a process for maintaining documents in the Design History File.	31-Dec-17		Design Controls		
CAP	[redacted] (b) (4) will be assessed for Part 11 compliance.	30-Mar-18		Validation		
CAP	Risk Management Program will be updated to include periodic review of risk assessments.	30-Mar-18		Quality Systems		

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	An overarching system is to be established which governs Design Control at the site. This is to include processes to manage Devices at the site along with document creation, modification, review, approval and storage of Design History Files related system for Design Control	30-Mar-18		Design Controls		
Compliance Action Plan – Product Complaint System Assessment						
CAP	SOP-QLE-SQC-00702, Product Complaint Handling, will be updated for additional clarity and work instructions.	30-Nov-17		Complaints		
CAP	SOP-DVL-PDV-10767, Product Technology Internal Investigation Logbook, and LOG-DVL-PDV-10762, Internal Investigation Logbook, will be updated to include the logging of complaint samples.	30-Nov-17		Complaints		
CAP	SOP-QLC-SQC-11012, Auto-Injector Functionality Sample Transfer from QA Floor to QC Devices Lab, will be updated to include the logging of complaint samples.	30-Nov-17		Complaints		
Compliance Action Plan – Investigation Systems Assessment						
CAP	SOP-QLA-MQA-00720, Event and Deviation Reporting (ER & QAR), will be updated for additional clarity, work instructions and Method 1 requirement.	30-Nov-17		Quality Systems		
CAP	SOP-QLA-MQA-00001, Laboratory Investigation will be updated for additional clarity, work instructions, and consistency of notification timeline. And evaluation against FDA Guidance for Industry, Investigation Out-of-Specification (OOS) Test Results for Pharmaceutical Production.	30-Nov-17		Laboratory		
CAP	SOP-LAB-GEN-11113, Evaluation and Trending Of Laboratory Investigation Report Causes, will be updated to include the use of the electronic commitment tracking system for issuance of (b) (4) laboratory trend reports.	30-Nov-17		Laboratory		
CAP	To ensure definition consistency across GMP documents and all departments, a site wide glossary will be compiled.	18-Dec-17		Quality Systems		

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	Develop new procedure for Standard Operation Procedure (SOP) design elements.	18-Dec-17		Quality Systems		
Compliance Action Plan – Corrective Actions and Preventative Actions Systems Assessment						
CAP	SOP-QLA-MQA-00720, Event and Deviation Reporting (ER & QAR), will be updated to ensure each unplanned subject to GMP activities is treated as a discrete incident.	30-Nov-17		Quality Systems		
CAP	Develop and approve an SOP to document statistical methodology utilized at the site. This SOP will include trending methodology, definitions, how to conduct trend analysis, detection of recurring quality issues, and instructions for CAPA requirements.	01-Mar-18		Quality Systems		
CAP	SOP-QLA-MQA-00738, Regulatory Agency Inspection and Contacts, will be updated to state the requirement for regulatory commitments to be tracked in the Commitment Tracking module of (b) (4)	01-Mar-18		Quality Systems		
CAP	Supplier Corrective Action Request (SCAR) process and SOP-QLC-QLE-00008, Supplier Corrective Action Request will be updated to align roles and responsibilities, quality approval, and clarification.	30-Apr-18		Quality Systems		
CAP	SOP-QLA-MQA-00749, Corrective and Preventive Action (CAPA) Program, will be updated to clarify requirements for effectiveness checks to align with 21 CFR820.100	01-May-18		Quality Systems		
Compliance Action Plan – Management Controls Assessment						
CAP	Meridian will update the Quality Manual to comply with the required elements to demonstrate compliance to 21 CFR Part 4, and will adopt a Quality Policy consistent and aligned with the Pfizer Quality Policy and update Site Quality Unit Roles and Responsibilities. The revised Quality Manual will be approved by Management with Executive Responsibility.	15-Feb-18		Quality Systems		
CAP	Procedure SOP-QLA-MQA-00006 will be updated to enhance Management Review and ensure the meeting content aligns with the requirements in 21 CFR 820.20(c).	28-Feb-18		Quality Systems		

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	SOP-QLA-MQA-00015, Meridian Drug Products (MDP) Risk Management Process, will be updated for clarification provided for scope of procedure. Associated procedure, SOP-QLA-GEN-00806, will be reviewed and either updated or obsoleted	28-Mar-18		Quality Systems		
CAP	SOP-QLA-MQA-00720, Event and Deviation Reporting (ER & QAR), SOP-QLC-QLE-00702, Product Complaint Handling, will be updated to define the links between the processes described in the SOPs and the use of the Risk Management File.	29-Mar-19		Quality Systems		
Compliance Action Plan – Purchasing Controls Assessment						
CAP	Revise 7023010C-QC, NGA Power Pak Assembly Quality Control Test Report to require ANSI/ASQz1.4-2003, Level II sampling plan	31-Jan-18		Quality Systems		
CAP	SOP-QLA-COM-00012, Supplier Performance Rating Procedure, will be revised to clarify scope of vendors and clarification on CAPA requirements	30-Apr-18		Quality Systems		
CAP	SOP-QLA-MQA-00006, Site Quality Review Team, will be updated to increase frequency of Vendor Quality Management Review and as determined by Management during the Management Review meetings, further action may be taken in response to poor Vendor quality ratings.	30-Apr-18		Quality Systems		

Exhibit 2. Compliance Action Plan (CAP) dashboard (last updated October 30, 2017)

Exhibit 3. EPIPEN NGA DESIGN CONTROL VERIFICATION SCHEDULE (as of October 31, 2017)

ACTIVITY	COMPLETE DATE
DEFINE USER NEEDS	
Perform Comprehensive Review of User Needs (incl. Focus Groups, Complaints Review, and Post-Market Surveillance/ Literature Data Review)	FEB 2018
REVIEW & UPDATE DESIGN INPUTS	
Update User Requirements Specifications & Product Requirements Specifications (URS/PRS) to: • Provide consistency between the product requirements section and the technical requirements section • Provide a [redacted (b) (4)] for essential to functional attributes, based on User/Patient needs and to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability	FEB 2018
REVIEW & UPDATE DESIGN OUTPUTS	
Review Inspection Criteria and Sampling Plans (QC Test Reports, SQPs)	DEC 2017
Review Component Drawings and Specifications	DEC 2017
Evaluate If Risk Control Within the Supply Chain Supports Recommended System Level Reliability	DEC 2017
REVIEW & UPDATE RISK MANAGEMENT FILE	
Update Risk Management File Analyses Provide consistency between the product requirements section and the technical requirements section • User Task Analysis • HAL • uFMEA • dFMEA	FEB 2018

ACTIVITY	COMPLETE DATE
REVIEW & UPDATE DESIGN VERIFICATION	
Execute Design Verification Activities (incl. sequential preconditioning): • Create and Approve Protocol • Manufacture Batches • Conduct Testing at: (b) (4) • Complete Design Verification Summary Report, including (b) (4)	DEC 2018 (b) (4) (b) (4) JUL 2020 (b) (4)
REVIEW & UPDATE PROCESS VALIDATION	
Perform Process FMEA	MAR 2018
REVIEW & UPDATE DESIGN VALIDATION	
Complete HFE/UE Formative Studies	FEB 2018
Submit Draft HF Summative Validation Protocol to FDA for Review and Comments	MAR 2018
Execution of HF Summative Validation Study	OCT 2018
Submit Overall Design Validation Summary Report including HFE/UE Report summarizing all human factors and usability engineering work including the human factors validation study to FDA	JAN 2019